

**REMARKS**

Claims 1-4, 7-11, 13-30 are pending in this case. Claims 3, 4, 7-10 and 15-29 were previously withdrawn from consideration as being directed to a non-elected invention. Claims 5 and 31 were previously canceled. Claims 6, 12 and 11-14 are being cancelled herewith. Applicants are currently amending herewith Claims 1, 2, 7-10, and 29-30. Applicants submit that Claims 2 and 7-10 were improperly withdrawn from consideration and should be currently examined. Thus, Claims 1-2, 7-10, and 29-30 remain for consideration.

**The Office Action**

Claims 1, 6, 12 and 30 were rejected under 35 U.S.C. § 102(e) as being completely anticipated and unpatentable over the patent to Sachdeva et al. (U.S. Patent No. 6,054,598). Claims 1, 6 and 30 were rejected under 35 U.S.C. § 102(e) as being completely anticipated and unpatentable over the patent to Ram et al. (U.S. Patent No. 6,136,992). Claims 1 was rejected under 35 U.S.C. § 102(b) as being completely anticipated in view of the article by Lovely et al. Claims 1, 2, 3, 4, 11, 13, 14 and 30 were rejected under 35 U.S.C. § 103(a) as being obvious and unpatentable over the patent to Ram et al. Claims 1, 6, 12 and 30 were rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claims 1, 6, 12 and 30 were also rejected under 35 U.S.C. § 112, second paragraph as being indefinite. Applicants respectfully traverse these rejections.

**Claim Rejections under 35 U.S.C. § 102(e) in View of Sachdeva et al.**

Claims 1, 6, 12, and 30 were rejected in the Office Action of November 29, 2002, as being anticipated under 35 U.S.C. § 102(e) by U.S. Patent No. 6,054,598 to Sachdeva et al. (“Sachdeva”). It is the Examiner’s position that Sachdeva discloses both 2-ethoxyestradiol ( $R_a$  is  $-OCH_2CH_3$ ) and 2-(2’,2’,2’-trifluoroethoxy)estradiol ( $R_a$  is  $-OCH_2CF_3$ ) and therefore anticipates these claims. Applicants respectfully assert that this rejection has been obviated for each of Claims 1, 6, 12, and 30 by the amendments herein, as follows.

Claim 1 is amended herein to recite the proviso that  $R_1$  is not  $-CF_3$ . This proviso therefore, excludes 2-(2’,2’,2’-trifluoroethoxy)estradiol ( $R_a$  is  $-OCH_2CF_3$ ). The proviso of Claim 1 further provides that  $R_a$  is not  $-OR$  which thereby excludes 2-methoxyestradiol and 2-ethoxyestradiol.

Claims 6 and 12 are cancelled by the amendment herein, thereby obviating the rejection of these claims in view of Sachdeva.

Claim 30 is amended herein to recite the proviso that  $R_1$  is not  $-CF_3$ . This proviso excludes 2-(2’,2’,2’-trifluoroethoxy)estradiol ( $R_a$  is  $-OCH_2CF_3$ ) from this claim. The selection of  $R_a = OCH_3$  or  $-OCH_2CH_3$  are not possible options for  $R_a$  in Claim 30.

Applicants respectfully assert that this rejection has been obviated for each of Claims 1 and 30 by the amendments herein, and therefore request withdrawal of this rejection and allowance of these claims.

**Claim Rejections under 35 U.S.C. § 102(e) in View of D’Amato et al.**

Claims 1, 6, 12, and 30 also appear to be rejected in the November 29, 2002, Office Action as being anticipated under 35 U.S.C. § 102(e) by U.S. Patent No. 5,504,074 to

D'Amato et al. ("D'Amato"). It appears to be the Examiner's position that these claims are anticipated by the first two compounds of Table 2, namely, 2-methoxyestradiol and 2-methoxyestrone. The Examiner also cites Table 1, lines 32, 37, 38 and 41 (column 8) against Claims 1, 6, 12, and 30. Applicants note that this rejection was fully addressed in their response filed June 13, 2002, however in order to expedite examination of this application, Applicants will repeat their arguments.

Applicants note, as they did in their response filed June 13, 2002, that the specific compounds of D'Amato's Table 1 to which the Examiner refers can not be determined unambiguously. However, it is Applicants' belief that the Examiner refers to the following species of Table 1: 2-methoxyestradiol, estradiol, estrone, and 2-methoxyestradiol-3-O-methylether. Applicants respectfully traverse this rejection with respect to Claims 1 and 30 as follows. Further, Applicants' cancellation of Claims 6 and 12 has obviated this rejection with respect to these claims.

2-Methoxyestradiol. As amended, Claim 1 recites the proviso that R<sub>a</sub> is not -OR. This proviso specifically excludes 2-methoxyestradiol from Claim 1, while the definition of R<sub>a</sub> = -OCH<sub>3</sub> is not possible in 30. Therefore, neither Claims 1 nor 30 read on this compound in Table 1 of D'Amato.

Estradiol. This compound requires R<sub>a</sub> to be a hydrogen atom, which is bonded to the C2 position of the steroid A-ring. Applicants respectfully note that neither Claim 1 nor 30 defines R<sub>a</sub> as hydrogen, and, therefore, these claims are not anticipated by this compound in Table 1 of D'Amato.

Estrone. This compound also requires R<sub>a</sub> to be a hydrogen atom, which is bonded to the C2 position of the steroid structure. Applicants respectfully note that neither Claim 1 nor

30 defines R<sub>a</sub> as hydrogen, and, therefore, these claims are not anticipated by this compound in Table 1 of D'Amato.

2-Methoxyestradiol-3-O-methylether. This compound requires Z' to be >CO-CH<sub>3</sub>, in which a methyl ether moiety is bonded at the C3 position of the steroid structure. Applicants respectfully note that neither Claim 1 nor 30 defines Z' as >CO-CH<sub>3</sub>, and, therefore, these claims are not anticipated by this compound in Table 1 of D'Amato.

Applicants maintain that none of the cited compounds in Table 1 of D'Amato anticipate Claims 1 or 30, and, accordingly, Applicants respectfully request withdrawal of this rejection, and allowance of these claims.

**Claim Rejections under 35 U.S.C. § 102(b) in View of Ram et al.**

Claims 1, 6, and 30 were rejected in the Office Action of November 29, 2002, as being anticipated under 35 U.S.C. § 102(b) by U.S. Patent No. 6,136,992 to Ram et al. ("Ram"). It is the Examiner's position that Ram discloses 2-(2',2',2'-trifluoroethoxy)estradiol (R<sub>a</sub> is -OCH<sub>2</sub>CF<sub>3</sub>) and therefore anticipates these claims.

Applicants respectfully assert that Ram does not constitute prior art under 35 U.S.C. § 102(b). The issue date of U.S. Patent No. 6,136,992 to Ram is October 24, 2000, which is after the filing date of the present application. The present application is a continuation of U.S. Patent Application Serial No. 09/154,322, filed September 16, 1998, which claims the benefit of U.S. Provisional Application No. 60/059,916, filed September 24, 1997.

Nonetheless, Applicants respectfully assert that even if this rejection was made on the basis of 35 U.S.C. § 102(e), it has been obviated for each of Claims 1 and 30 by the amendments herein, for the following reasons.

Claim 1 is amended herein to recite the proviso that R<sub>a</sub> is not -OR and R<sub>1</sub> is not -CF<sub>3</sub>. This proviso therefore, excludes 2-(2',2',2'-trifluoroethoxy)estradiol (R<sub>a</sub> is -OCH<sub>2</sub>CF<sub>3</sub>) along with 2-methoxyestradiol and 2-ethoxyestradiol.

Claim 6 is cancelled by the amendment herein, thereby obviating any rejection of this claim in view of Ram.

Claim 30 is amended herein to recite the proviso that R<sub>1</sub> is not -CF<sub>3</sub>. This proviso excludes 2-(2',2',2'-trifluoroethoxy)estradiol (R<sub>a</sub> is -OCH<sub>2</sub>CF<sub>3</sub>) from this claim.

Applicants respectfully assert that any rejection in view of Ram has been obviated for each of Claims 1 and 30 by the amendments herein, and, therefore, request withdrawal of this rejection and allowance of these claims.

**Claim Rejection under 35 U.S.C. § 102(b) in View of Lovely et al.**

In the Office Action dated June 4, 2003, Claim 1 was rejected under 35 U.S.C. § 102(b) as being completely anticipated in view of the article by Lovely et al. The rejection references compounds 1, 2 and 3 on page 1917 of Lovely et al., where X can be OH; CH<sub>2</sub>OH and CH<sub>2</sub>CH<sub>2</sub>OH. The rejection states that these compounds are claimed in the present application when R<sub>g</sub> is OH; Z' is CH<sub>2</sub>; Z' is OH; R<sub>a</sub> and R<sub>b</sub> [*sic.*, R<sub>b</sub> and R<sub>o</sub>] are H and R<sub>a</sub> is R-R<sub>1</sub>. Applicants respectfully assert that this rejection has been obviated by the amendment of Claim 1 herein, as follows.

Claim 1 is amended herein to recite the proviso that R<sub>a</sub> is not -OR and R<sub>1</sub> is not -OH. This proviso therefore excludes 2-(hydroxyalkyl) estradiols.

Since Lovely et al. does not disclose each and every feature of Claim 1, Lovely et al. cannot anticipate Claim 1. Applicants respectfully assert that this rejection has been obviated for Claim 1 by the amendments herein, and therefore request withdrawal of this rejection and allowance of this claim and all claims dependent thereon.

**Claim Rejection under 35 U.S.C. § 103(a) in View of Ram et al.**

In the Office Action dated June 4, 2003, Claims 1, 2, 3, 4, 11, 13, 14 and 30 were rejected under 35 U.S.C. § 103(a) as being obvious and unpatentable over the patent to Ram et al. The rejection states that Ram et al. teaches 2-alkoxy estradiol derivatives that embrace the presently claimed invention. The rejection further states that the present invention differs from the reference in claiming a broader scope. The rejection concludes that the instant claims are considered obvious in view of Ram et al. which discloses that R3 represents C=N-OH or C=N-O-lower alkyl; R1 is substituted or unsubstituted lower alkyl group; and R2 is OH. Applicants respectfully assert that this rejection has been obviated by the amendment of Claims 1 and 30 herein, as follows.

Ram et al. discloses estradiol compounds that must be substituted at the “2” position by alkoxy groups or substituted alkoxy groups of C1-C6. Claims 1 and 30 are amended herein to recite the proviso that R<sub>a</sub> is not -OR. This proviso therefore excludes the 2-alkoxy estradiol derivatives disclosed by Ram et al. Ram et al. does not disclose or suggest the other substituents presently claimed. Therefore, the present claims are not obvious in view of Ram et al.

Applicants respectfully assert that any rejection in view of Ram has been obviated for each of Claims 1 and 30, as well as the dependent claims that depend therefrom, by the

amendments herein, and therefore request withdrawal of this rejection and allowance of these claims.

**Claim Rejections under 35 U.S.C. § 112, First Paragraph**

In the Office Action of November 29, 2002, Claims 1, 6, 12, and 30 were rejected under 35 U.S.C. § 112, first paragraph, as lacking a written description. It is the Examiner's position that the proviso related to disclaimed compounds of Claims 1 and 30 has no support in the disclosure, and therefore that this proviso constitutes new matter.

Claims 6 and 12 are cancelled by the amendment herein, thereby obviating the rejection of these claims under 35 U.S.C. § 112, first paragraph. Applicants respectfully traverse this rejection for Claims 1 and 30 for the following reasons.

Applicants have searched the MPEP with respect to provisos which exclude subject matter, such as those of Claims 1 and 30, and have found no section that prohibits their use. As set forth in MPEP § 2173.05(i), “[i]f alternative elements are positively recited in the specification, they may be **explicitly excluded** in the claims.” (Emphasis added). Applicants respectfully maintain that alternative elements are positively recited in the specification, as alternative definitions of R<sub>a</sub> provided therein. *See*, for example, specification page 15, lines 9-12, and in the individual compounds disclosed in Table 3, page 18 and in Table 1, page 13. Accordingly, Applicants respectfully assert that any of these alternative definitions of R<sub>a</sub> may be **explicitly excluded** in the claims according to MPEP § 2173.05(i), as Applicants have done in Claims 1 and 30.

The only requirement of the MPEP for a proviso to meet the requirements of 35 U.S.C. § 112, first paragraph, is that “[a]ny claim containing a negative limitation *which does not*

*have basis in the original disclosure* should be rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement.” Emphasis added; MPEP § 2173.05(i). Applicants respectfully assert that the individual features of Claims 1 and 30, namely, the **alternative definitions of Ra**, have a basis in the original disclosure. (See, for example, specification page 15, lines 9-12; Table 3, page 18; Table 1, page 13). The lack of a literal basis for a proviso, by itself, is not sufficient to establish a *prima facie* case for lack of descriptive support. MPEP § 2173.05(i); *Ex parte Parks* 30 USPQ2d 1234, 1236 (Bd. Pat. App. & Inter. 1993).

The Federal Circuit has addressed this specific Section 112, first paragraph, issue in *In re Johnson and Farnham* 194 USPQ 187 (CCPA 1977), where the Court posed, “[t]he only inquiry is whether, after exclusion from the original claim of two species specifically disclosed in the 1963 application, the 1963 disclosure satisfies § 112, first paragraph, for the ‘limited genus’ now claimed.” The *In re Johnson* Court held that the original claim, *with two species excepted out, satisfied* the requirements of 35 U.S.C. § 112, first paragraph, noting that, “...appellants are merely excising the invention of another, to which they are not entitled, and are not creating an ‘artificial subgenus’ or claiming ‘new matter.’” *In re Johnson* at 196.

Applicants respectfully maintain that, for the reasons provided herein and in *In re Johnson*, the provisos of Claims 1 and 30 that remove *some* compounds do not introduce new matter into these claims. Instead, the provisos of Claims 1 and 30 merely reflect the Applicants’ “claiming less than the full scope of [their] disclosure.” *In re Johnson* at 196; emphasis in original. Applicants respectfully assert that patent applicants frequently discover during the course of prosecution that only a part of what they originally claimed is patentable, but “[i]t is for

the inventor to decide what *bounds* of protection he will seek.” *In re Johnson* at 196; emphasis in original.

Accordingly, Applicants respectfully assert that Claims 1 and 30 are fully enabled under 35 U.S.C. § 112, first paragraph, and request withdrawal of this rejection and allowance of these claims.

#### **Claim Rejections under 35 U.S.C. § 112, Second Paragraph**

Claims 1, 6, 12, and 30 were rejected in the Office Action of November 29, 2002, as being indefinite under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention. It is the Examiner’s position that the feature >C-R<sub>2</sub>-OH in Claims 1 and 30 is unclear, and clarification is required.

Claims 6 and 12 are cancelled by the amendment herein, thereby obviating any rejection of these claims under 35 U.S.C. § 112, Second Paragraph.

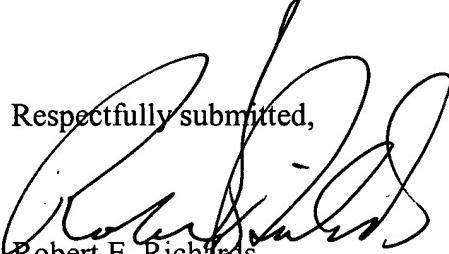
The claim feature >C-R<sub>2</sub>-OH appears in Claims 1 and 30 in the definition of Z’, wherein R<sub>2</sub> is defined as an alkyl or branched alkyl with up to 10 carbons or aralkyl. Thus, R<sub>2</sub> constitutes an alkyl, branched alkyl, or aralkyl linker between the benzene ring carbon (specified as >C) and the hydroxy group. Examples of >C-R<sub>2</sub>-OH groups that fall into this definition include, but are not limited to >CCH<sub>2</sub>OH, >CCH<sub>2</sub>CH<sub>2</sub>OH, >CCH<sub>2</sub>CH(CH<sub>3</sub>)OH, >CCH<sub>2</sub>(4-C<sub>6</sub>H<sub>4</sub>OH), >CCH<sub>2</sub>(2-C<sub>6</sub>H<sub>4</sub>OH), and the like. Support for this feature is found in the specification on page 15, lines 14-15, and in Table 1 page 13. Nevertheless, applicants are amending Claims 1 and 30 herewith to remove the feature >C-R<sub>2</sub>-OH, thereby obviating this rejection.

Accordingly, Applicants respectfully assert that Claims 1 and 30 are definite under 35 U.S.C. § 112, second paragraph, and request withdrawal of this rejection and allowance of these claims.

**Conclusion**

In view of the foregoing amendments and remarks, applicants maintain that the present application is in condition for allowance. Such action is respectfully requested. If the Examiner believes there are any other issues that may be resolved by telephone interview, examiner's amendment or otherwise, a telephone call to the undersigned attorney at (404) 815-6500 is courteously solicited.

Respectfully submitted,

  
Robert E. Richards  
Reg. No. 29,105

Kilpatrick Stockton LLP  
1100 Peachtree Street, Suite 2800  
Atlanta, Georgia 30309-4530  
(404) 815-6500  
Our Docket: 05213-0910 (43170-260981)